

SEQUENCE LISTING

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Ser Cys Pro Asn Gly Ser Cys Trp Gly Gly Glu Glu Asn Cys Gln
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Met	Tyr	Asn	Asn	Cys	Glu	Val	Val	Leu	Gly	Asn	Leu	Glu	Ile	Thr	Tyr	
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Ala	Gly	Tyr	Val	Leu	Ile	Ala	Leu	Asn	Thr	Val	Glu	Arg	Ile	Pro	Leu	
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Glu	Asn	Leu	Gln	Ile	Ile	Arg	Gly	Asn	Ala	Leu	Tyr	Glu	Asn	Thr	Tyr	
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gcc	tta	gcc	atc	ctg	tcc	aac	tat	ggg	aca	aac	aga	act	ggg	ctt	agg	675
Ala	Leu	Ala	Ile	Leu	Ser	Asn	Tyr	Gly	Thr	Asn	Arg	Thr	Gly	Leu	Arg	
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Glu	Leu	Pro	Met	Arg	Asn	Leu	Gln	Glu	Ile	Leu	Ile	Gly	Ala	Val	Arg	
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ttc	agc	aa	ac	cc	atc	ctc	tgc	aat	atg	gat	act	atc	cag	tgg	agg	775

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Ser His Pro Ser Ser Cys Pro Lys Cys Asp Pro Ser Cys Pro Asn Gly		
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Ser Cys Trp Gly Gly Glu Asn Cys Gln Lys Thr Lys Ile		
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Ile Cys Ala Gln Gln Cys Ser His Arg Cys Arg Gly Arg Ser Pro Ser		
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Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His Gly Ser Cys Val Arg		
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Val Ala Phe Lys Gly Asp Ser Phe Thr Arg Thr Pro Pro Leu Asp Pro		
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Ile Pro Val Ala Ile Lys Glu Leu Arg Glu Ala Thr Ser Pro Lys Ala		
745 750 755		
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Glu His Lys Asp Asn Ile Gly Ser Gln Tyr Leu Leu Asn Trp Cys Val		
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<400> 6

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35 40 45

Leu Ser Leu Gln Arg Met Tyr Asn Asn Cys Glu Val Val Leu Gly Asn
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Thr Ile Gln Glu Val Ala Gly Tyr Val Leu Ile Ala Leu Asn Thr Val
85 90 95

Glu Arg Ile Pro Leu Glu Asn Leu Gln Ile Ile Arg Gly Asn Ala Leu
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Tyr Glu Asn Thr Tyr Ala Leu Ala Ile Leu Ser Asn Tyr Gly Thr Asn
115 120 125

Arg Thr Gly Leu Arg Glu Leu Pro Met Arg Asn Leu Gln Glu Ile Leu
130 135 140

Ile Gly Ala Val Arg Phe Ser Asn Asn Pro Ile Leu Cys Asn Met Asp
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180 185 190

Ser Cys Pro Asn Gly Ser Cys Trp Gly Gly Glu Asn Cys Gln
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Lys Leu Thr Lys Ile Ile Cys Ala Gln Gln Cys Ser His Arg Cys Arg
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Gly Arg Ser Pro Ser Asp Cys Cys His Asn Gln Cys Ala Ala Gly Cys
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Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val Val Thr Asp His
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Gly Ser Cys Val Arg Ala Cys Gly Pro Asp Tyr Tyr Glu Val Glu Glu
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Asp Gly Ile Arg Lys Cys Lys Cys Asp Gly Pro Cys Arg Lys Val
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Cys Asn Gly Ile Gly Ile Gly Glu Phe Lys Asp Thr Leu Ser Ile Asn
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Ala Thr Asn Ile Lys His Phe Lys Tyr Cys Thr Ala Ile Ser Gly Asp
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Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr Lys Gln
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His Gly Gln Phe Ser Leu Ala Val Val Gly Leu Asn Ile Thr Ser Leu
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Ser Gly Pro Lys Ile Pro Ser Ile Ala Thr Gly Ile Val Gly Leu
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 660 665 670

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 675 680 685

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Ser Leu Ser Ala Thr Ser Asn Asn Ser Thr Val Ala Cys Ile Asn
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Arg Asn Gly Ser Cys Arg Val Lys Glu Asp Ala Phe Leu Gln Arg
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Tyr Ser Ser Asp Pro Thr Gly Ala Val Thr Glu Asp Asn Ile Asp
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Asp Ala Phe Leu Pro Val Pro Glu Tyr Val Asn Gln Ser Val Pro
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Lys Arg Pro Ala Gly Ser Val Gln Asn Pro Val Tyr His Asn Gln
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Pro Leu His Pro Ala Pro Gly Arg Asp Leu His Tyr Gln Asn Pro
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His Ser Asn Ala Val Gly Asn Pro Glu Tyr Leu Asn Thr Ala Gln
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Pro Thr Cys Leu Ser Ser Gly Phe Asn Ser Pro Ala Leu Trp Ile
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Gln Lys Gly Ser His Gln Met Ser Leu Asp Asn Pro Asp Tyr Gln
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Gln Asp Phe Phe Pro Lys Glu Thr Lys Pro Asn Gly Ile Phe Lys
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Ser Ser Glu Phe Ile Gly Ala
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18

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cccacggggc ccttactgc gccgcgcgcc cggcccccac ccctcgccgc accccgcgc	180
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atg gag ctg gcg gcc ttg tgc cgc tgg ggg ctc ctc ctc gcc ctc ttg	286
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu	
1 5 10 15	
ccc ccc gga gcc gcg agc acc caa gtg tgc acc ggc aca gac atg aag	334
Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys	
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ctg cgg ctc cct gcc agt ccc gag acc cac ctg gac atg ctc cgc cac	382
Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His	
35 40 45	
ctc tac cag ggc tgc cag gtg gtg cag gga aac ctg gaa ctc acc tac	430
Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr	
50 55 60	
ctg ccc acc aat gcc agc ctg tcc ttc ctg cag gat atc cag gag gtg	478
Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val	
65 70 75 80	
cag ggc tac gtg ctc atc gct cac aac caa gtg agg cag gtc cca ctg	526
Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu	
85 90 95	
cag agg ctg cgg att gtg cga ggc acc caa gtg ctc ttt gag gac aac tat	574
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr	
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gcc ctg gcc gtg cta gac aat gga gac ccc ctg aac aat acc acc cct	622
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro	
115 120 125	
gtc aca ggg gcc tcc cca gga ggc ctg cgg gag ctg cag ctt cga agc	670
Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser	
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Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln	
145 150 155 160	
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Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn	
165 170 175	
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Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys	

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tct gag gat tgt cag acg ctg acg cgc act gtc tgt gcc ggt ggc tgt Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys 210 215 220			910
gcc cgc tgc aag ggg cca ctg ccc act gac tgc tgc cat gag cag tgt Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys 225 230 235 240			958
gct gcc ggc tgc acg ggc ccc aag cac tct gac tgc ctg gcc tgc ctc Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu 245 250 255			1006
cac ttc aac cac agt ggc atc tgt gag ctg cac tgc cca gcc ctg gtc His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val 260 265 270			1054
acc tac aac aca gac acg ttt gag tcc atg ccc aat ccc gag ggc cgg Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg 275 280 285			1102
tat aca ttc ggc gcc agc tgt gtg act gcc tgt ccc tac aac tac ctt Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu 290 295 300			1150
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cca gcc tcc aac act gcc ccg ctc cag cca gag cag ctc caa gtg ttt Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe 385 390 395 400			1438
gag act ctg gaa gag atc aca ggt tac cta tac atc tca gca tgg ccg Glu Thr Leu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro 405 410 415			1486
gac agc ctg cct gac ctc agc gtc ttc cag aac ctg caa gta atc cgg Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg 420 425 430			1534
gga cga att ctg cac aat ggc gcc tac tcg ctg acc ctg caa ggg ctg Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu 435 440 445			1582
ggc atc agc tgg ctg ggg ctg cgc tca ctg agg gaa ctg ggc agt gga Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly			1630

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ctg gcc ctc atc cac cat aac acc cac ctc tgc ttc gtg cac acg gtc Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val			1678
465 470 475 480			
ccc tgg gac cag ctc ttt cgg aac ccg cac caa gct ctg ctc cac act Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr			1726
485 490 495			
gcc aac ccg cca gag gac gag tgt gtg ggc gag ggc ctg gcc tgc cac Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His			1774
500 505 510			
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515 520 525			
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545 550 555 560			
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565 570 575			
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580 585 590			
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595 600 605			
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610 615 620			
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625 630 635 640			
ggc tgc ccc gcc gag cag aga gcc agc cct ctg acg tcc atc atc tct Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser			2206
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675 680 685			
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690 695 700			
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705 710 715 720			
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725	730	735	
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aaa gtg ttg agg gaa aac aca tcc ccc aaa gcc aac aaa gaa atc tta Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu 755	760	765	2542
gac gaa gca tac gtg atg gct ggt gtg ggc tcc cca tat gtc tcc cgc Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg 770	775	780	2590
ctt ctg ggc atc tgc ctg aca tcc acg gtg cag ctg gtg aca cag ctt Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu 785	790	795	2638
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ctg ggc tcc cag gac ctg ctg aac tgg tgt atg cag att gcc aag ggg Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly 820	825	830	2734
atg agc tac ctg gag gat gtg cgg ctc gta cac agg gac ttg gcc gct Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala 835	840	845	2782
cgg aac gtg ctg gtc aag agt ccc aac cat gtc aaa att aca gac ttc Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe 850	855	860	2830
ggg ctg gct cgg ctg ctg gac att gac gag aca gag tac cat gca gat Gly Leu Ala Arg Ile Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp 865	870	875	2878
ggg ggc aag gtg ccc atc aag tgg atg gcg ctg gag tcc att ctc cgc Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg 885	890	895	2926
cgg cgg ttc acc cac cag agt gat gtg tgg agt tat ggt gtg act gtg Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val 900	905	910	2974
tgg gag ctg atg act ttt ggg gcc aaa cct tac gat ggg atc cca gcc Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala 915	920	925	3022
cgg gag atc cct gac ctg ctg gaa aag ggg gag cgg ctg ccc cag ccc Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro 930	935	940	3070
ccc atc tgc acc att gat gtc tac atg atc atg gtc aaa tgt tgg atg Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met 945	950	955	3118
att gac tct gaa tgt cgg cca aga ttc cgg gag ttg gtg tct gaa ttc Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe 965	970	975	3166
tcc cgc atg gcc agg gac ccc cag cgc ttt gtg gtc atc cag aat gag Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu 980	985	990	3214
gac ttg ggc cca gcc agt ccc ttg gac agc acc ttc tac cgc tca ctg Asp Leu Gly Pro Ala Ser Pro Leu Asp Ser Thr Phe Tyr Arg Ser Leu 980			3262

995	1000	1005	
ctg gag gac gat gac atg ggg	gac ctg gtg gat gct	gag gag tat	3307
Leu Glu Asp Asp Asp Met Gly	Asp Leu Val Asp Ala	Glu Glu Tyr	
1010	1015	1020	
ctg gta ccc cag cag ggc ttc	tcc tgt cca gac cct	gcc ccg ggc	3352
Leu Val Pro Gln Gln Gly Phe	Phe Cys Pro Asp Pro	Ala Pro Gly	
1025	1030	1035	
gct ggg ggc atg gtc cac cac	agg cac cgc agc tca	tct acc agg	3397
Ala Gly Gly Met Val His His	Arg His Arg Ser Ser	Ser Thr Arg	
1040	1045	1050	
agt ggc ggt ggg gac ctg aca	cta ggg ctg gag ccc	tct gaa gag	3442
Ser Gly Gly Asp Leu Thr	Leu Gly Leu Glu Pro	Ser Glu Glu	
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gag gcc ccc agg tct cca ctg	gca ccc tcc gaa ggg	gct ggc tcc	3487
Glu Ala Pro Arg Ser Pro Leu	Ala Pro Ser Glu Gly	Ala Gly Ser	
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Asp Val Phe Asp Gly Asp Leu	Gly Met Gly Ala Ala	Lys Gly Leu	
1085	1090	1095	
caa agc ctc ccc aca cat gac	ccc agc cct cta cag	cgg tac agt	3577
Gln Ser Leu Pro Thr His Asp	Pro Ser Pro Leu Gln	Arg Tyr Ser	
1100	1105	1110	
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Glu Asp Pro Thr Val Pro Leu	Pro Ser Glu Thr Asp	Gly Tyr Val	
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Ala Pro Leu Thr Cys Ser Pro	Gln Pro Glu Tyr Val	Asn Gln Pro	
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Asp Val Arg Pro Gln Pro Pro	Ser Pro Arg Glu Gly	Pro Leu Pro	
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gct gcc cga cct gct ggt gcc	act ctg gaa agg ccc	aag act ctc	3757
Ala Ala Arg Pro Ala Gly Ala	Thr Leu Glu Arg Pro	Lys Thr Leu	
1160	1165	1170	
tcc cca ggg aag aat ggg gtc	gtc aaa gac gtt ttt	gcc ttt ggg	3802
Ser Pro Gly Lys Asn Gly Val	Val Lys Asp Val Phe	Ala Phe Gly	
1175	1180	1185	
ggt gcc gtg gag aac ccc gag	tac ttg aca ccc cag	gga gga gct	3847
Gly Ala Val Glu Asn Pro Glu	Tyr Leu Thr Pro Gln	Gly Gly Ala	
1190	1195	1200	
gcc cct cag ccc cac cct cct	cct gcc ttc agc cca	gcc ttc gac	3892
Ala Pro Gln Pro His Pro Pro	Pro Ala Phe Ser Pro	Ala Phe Asp	
1205	1210	1215	
aac ctc tat tac tgg gac gag	gac cca cca gag cgg	ggg gct cca	3937
Asn Leu Tyr Tyr Trp Asp Gln	Asp Pro Pro Glu Arg	Gly Ala Pro	
1220	1225	1230	
ccc agc acc ttc aaa ggg aca	cct acg gca gag aac	cca gag tac	3982
Pro Ser Thr Phe Lys Gly Thr	Pro Thr Ala Glu Asn	Pro Glu Tyr	
1235	1240	1245	
ctg ggt ctg gac gtg cca gtg	tga accagaaggc caagtccgca		4026
Leu Gly	Leu Asp Val Pro Val		

1250

1255

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<400> 11

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Leu	Arg	Leu	Pro	Ala	Ser	Pro	Glu	Thr	His	Leu	Asp	Met	Leu	Arg	His
35						40					45				

Leu	Tyr	Gln	Gly	Cys	Gln	Val	Val	Gln	Gly	Asn	Leu	Glu	Leu	Thr	Tyr
50					55				60						

Leu	Pro	Thr	Asn	Ala	Ser	Leu	Ser	Phe	Leu	Gln	Asp	Ile	Gln	Glu	Val
65						70		75		75			80		

Gln	Gly	Tyr	Val	Leu	Ile	Ala	His	Asn	Gln	Val	Arg	Gln	Val	Pro	Leu
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Gln	Arg	Leu	Arg	Ile	Val	Arg	Gly	Thr	Gln	Leu	Phe	Glu	Asp	Asn	Tyr
						100		105				110			

Ala	Leu	Ala	Val	Leu	Asp	Asn	Gly	Asp	Pro	Leu	Asn	Asn	Thr	Thr	Pro
						115			120			125			

Val	Thr	Gly	Ala	Ser	Pro	Gly	Gly	Leu	Arg	Glu	Leu	Gln	Leu	Arg	Ser
							130	135		140					

Leu	Thr	Glu	Ile	Leu	Lys	Gly	Gly	Val	Leu	Ile	Gln	Arg	Asn	Pro	Gln
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145	150	155	160
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165		170	175
Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys			
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His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser			
195	200		205
Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys			
210	215		220
Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys			
225	230	235	240
Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu			
245	250		255
His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val			
260	265		270
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg			
275	280		285
Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu			
290	295		300
Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln			
305	310	315	320
Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys			
325	330		335
Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu			
340	345		350
Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys			
355	360		365
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp			
370	375		380
Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe			
385	390	395	400
Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro			
405	410		415
Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg			

420

425

430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
 435 440 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
 450 455 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
 465 470 475 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
 485 490 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
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Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
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Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
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Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
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Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
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Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
 580 585 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
 595 600 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
 610 615 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
 625 630 635 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
 645 650 655

Ala Val Val Gly Ile Leu Leu Val Val Leu Gly Val Val Phe Gly
 660 665 670

Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
 675 680 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly

690

695

700

Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
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Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
 725 730 735

Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
 740 745 750

Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
 755 760 765

Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
 770 775 780

Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
 785 790 795 800

Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
 805 810 815

Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
 820 825 830

Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
 835 840 845

Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
 850 855 860

Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
 865 870 875 880

Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
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Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
 900 905 910

Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
 915 920 925

Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
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Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe

965

970

975

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Leu Arg Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His					
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Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr					
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Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Lys Tyr					
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Cys Pro Pro Cys Ala Pro Thr Cys Lys Asp Asn His Cys Trp Gly Glu	
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Ser Pro Glu Asp Cys Gln Ile Leu Thr Gly Thr Ile Cys Thr Ser Gly	
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Cys Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys	
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Lys Pro Cys Ala Gly Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg	
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Lys Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly	
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Phe Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp	
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cta agg aag ctg aag gtg ctt ggg tca gga gcc ttc ggc act gtc tac Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr 725 730 735			2387
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Leu His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu
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Arg Gly Arg Ile Leu His Asp Gly Ala Tyr Ser Leu Thr Leu Gln Gly
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Gly Leu Ala Leu Ile His Arg Asn Thr His Leu Cys Phe Val Asn Thr
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Cys Tyr Gly Ser Glu Ala Asp Gln Cys Glu Ala Cys Ala His Tyr Lys
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Asp Ser Ser Ser Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp
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725 730 735

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 980 985 990

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Asn Lys Arg Ala Met Arg Arg Tyr Leu Glu Arg Gly Glu Ser Ile Glu
675 680 685

Pro Leu Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe
690 695 700

Lys Glu Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe
705 710 715 720

Gly Thr Val His Lys Gly Val Trp Ile Pro Glu Gly Glu Ser Ile Lys
725 730 735

Ile Pro Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser
740 745 750

Phe Gln Ala Val Thr Asp His Met Leu Ala Ile Gly Ser Leu Asp His
755 760 765

Ala His Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln
770 775 780

Leu Val Thr Gln Tyr Leu Pro Leu Gly Ser Leu Leu Asp His Val Arg
785 790 795 800

Gln His Arg Gly Ala Leu Gly Pro Gln Leu Leu Leu Asn Trp Gly Val
805 810 815

Gln Ile Ala Lys Gly Met Tyr Tyr Leu Glu Glu His Gly Met Val His
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Arg Asn Leu Ala Ala Arg Asn Val Leu Leu Lys Ser Pro Ser Gln Val
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Gln Val Ala Asp Phe Gly Val Ala Asp Leu Leu Pro Pro Asp Asp Lys
850 855 860

Gln Leu Leu Tyr Ser Glu Ala Lys Thr Pro Ile Lys Trp Met Ala Leu
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Glu Ser Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser
885 890 895

Tyr Gly Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Glu Pro Tyr
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 Val Lys Cys Trp Met Ile Asp Glu Asn Ile Arg Pro Thr Phe Lys Glu
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 His Gly Leu Thr Asn Lys Lys Leu Glu Glu Val Glu Leu Glu Pro Glu
 995 1000 1005
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 Gly His Val Thr Gly Ser Glu Ala Glu Leu Gln Glu Lys Val Ser
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 1130 1135 1140
 Thr Pro Leu Ser Pro Pro Gly Leu Glu Glu Glu Asp Val Asn Gly
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 Tyr Val Met Pro Asp Thr His Leu Lys Gly Thr Pro Ser Ser Arg
 1160 1165 1170
 Glu Gly Thr Leu Ser Ser Val Gly Leu Ser Ser Val Leu Gly Thr
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Glu Glu Glu Asp Glu Asp Glu Glu Tyr Glu Tyr Met Asn Arg Arg
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Arg Arg His Ser Pro Pro His Pro Pro Arg Pro Ser Ser Leu Glu
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Glu Leu Gly Tyr Glu Tyr Met Asp Val Gly Ser Asp Leu Ser Ala
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Ser Leu Gly Ser Thr Gln Ser Cys Pro Leu His Pro Val Pro Ile
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Met Pro Thr Ala Gly Thr Pro Asp Glu Asp Tyr Glu Tyr Met
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 Ala Arg Gly Ser Glu Met Gly Asn Ser Gln Ala Val Cys Pro Gly Thr
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 Leu Asn Gly Leu Ser Val Thr Gly Asp Ala Asp Asn Gln Tyr Gln Thr
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96

144

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cga gaa gtg aca ggc tat gta ctg gtg gcc atg aat gaa ttc tct gta Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Val 85 90 95	288
ctg ccc tta cct aac ctc cga gtg gtc cgg gga acc cag gtc tac gat Leu Pro Leu Pro Asn Leu Arg Val Val Arg Gly Thr Gln Val Tyr Asp 100 105 110	336
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cat gag gct cat tgc ttc tcc tgc cat cca gaa tgc cag ccc atg gag His Glu Ala His Cys Phe Ser Cys His Pro Glu Cys Gln Pro Met Glu 545 550 555 560	1680
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gaa cta caa gac tgt tta ggc caa gca gag gta tta atg agc aaa cca Glu Leu Gln Asp Cys Leu Gly Gln Ala Glu Val Leu Met Ser Lys Pro 625 630 635 640	1920
cac ctg gtc ata gcg gtg aca gta gga ctg act gtg atc ttc ctg att His Leu Val Ile Ala Val Thr Val Gly Leu Thr Val Ile Phe Leu Ile 645 650 655	1968
ctg gga ggc tct ttt ctc tat tgg cgt gga cgc agg att cag aat aaa Leu Gly Gly Ser Phe Leu Tyr Trp Arg Gly Arg Arg Ile Gln Asn Lys 660 665 670	2016
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gac cca agc gag aag gca aac aaa gtc ttg gct aga atc ttc aaa gag Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe Lys Glu 690 695 700	2112
aca gag ctg agg aaa ctt aag gtg ctt ggc tct ggt gtc ttt gga act Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe Gly Thr 705 710 715 720	2160
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 Leu His Ser Glu Ala Lys Thr Pro Ile Lys Trp Met Ala Leu Glu Ser
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 atc cac ttt ggg aaa tac aca cac cag agt gat gtc tgg agt tac ggt 2688
 Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser Tyr Gly
 885 890 895
 gta acc gtt tgg gag ttg atg acc ttc ggg gca gag ccc tac gca ggg 2736
 Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Glu Pro Tyr Ala Gly
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 Leu Arg Leu Ala Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu
 915 920 925
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 aat gag ttt acc agg atg gcc cgg gac cca cca agg tat ctg gtc atc 2928
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Tyr His Ser Gln Arg His Ser	Leu Leu Thr Pro Val	Thr Pro Leu	
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Cys Pro Ala Ala Glu Gln Gly	Tyr Glu Glu Met Arg	Ala Phe Gln	
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Gly Pro Gly His Gln Ala Pro	His Val Arg Tyr Ala	Arg Leu Lys	
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Leu Tyr Lys Leu Tyr Glu Lys Cys Glu Val Val Met Gly Asn Leu Glu
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Ile Val Leu Thr Gly His Asn Ala Asp Leu Ser Phe Leu Gln Trp Ile
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Arg Glu Val Thr Gly Tyr Val Leu Val Ala Met Asn Glu Phe Ser Val
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Gly Lys Phe Ala Ile Phe Val Met Leu Asn Tyr Asn Thr Asn Ser Ser
 115 120 125

His Ala Leu Arg Gln Leu Arg Phe Thr Gln Leu Thr Glu Ile Leu Leu
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Gly Gly Val Tyr Ile Glu Lys Asn Asp Lys Leu Cys His Met Asp Thr
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Ile Asp Trp Arg Asp Ile Val Arg Val Pro Asp Ala Glu Ile Val Val
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Lys Asn Asn Gly Gly Asn Cys Pro Pro Cys His Glu Val Cys Lys Gly
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Arg Cys Trp Gly Pro Gly Pro Glu Asp Cys Gln Ile Leu Thr Lys Thr
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Ile Cys Ala Pro Gln Cys Asn Gly Arg Cys Phe Gly Pro Asn Pro Asn
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Gln Cys Cys His Asp Glu Cys Ala Gly Gly Cys Ser Gly Pro Gln Asp
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Thr Asp Cys Phe Ala Cys Arg His Phe Asn Asp Ser Gly Ala Cys Val
 245 250 255

Pro Arg Cys Pro Ala Pro Leu Val Tyr Asn Lys Leu Thr Phe Gln Leu
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Glu Pro Asn Pro His Ile Lys Tyr Gln Tyr Gly Gly Val Cys Val Ala
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Ser Cys Pro His Asn Phe Val Val Asp Gln Thr Phe Cys Val Arg Ala
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Cys Pro Ala Asp Lys Met Glu Val Asp Lys Asn Gly Leu Lys Met Cys
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Glu Pro Cys Arg Gly Leu Cys Pro Lys Ala Cys Glu Gly Thr Gly Ser
325 330 335

Gly Ser Arg Tyr Gln Thr Val Asp Ser Ser Asn Ile Asp Gly Phe Val
340 345 350

Asn Cys Thr Lys Ile Leu Gly Asn Leu Asp Phe Leu Ile Thr Gly Leu
355 360 365

Asn Gly Asp Pro Trp His Lys Ile Pro Ala Leu Asp Pro Glu Lys Leu
370 375 380

Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly Tyr Leu Asn Ile Gln
385 390 395 400

Ser Trp Pro Pro His Met His Asn Phe Ser Val Phe Ser Asn Leu Thr
405 410 415

Thr Ile Gly Gly Arg Ser Leu Tyr Asn Arg Gly Phe Ser Leu Leu Ile
420 425 430

Met Lys Asn Leu Asn Val Thr Ser Leu Gly Phe Arg Ser Leu Lys Glu
435 440 445

Ile Ser Ala Gly Arg Val Tyr Ile Ser Ala Asn Gln Gln Leu Cys Tyr
450 455 460

His His Ser Leu Asn Trp Thr Arg Leu Leu Arg Gly Pro Ala Glu Glu
465 470 475 480

Arg Leu Asp Ile Lys Tyr Asn Arg Pro Leu Gly Glu Cys Val Ala Glu
485 490 495

Gly Lys Val Cys Asp Pro Leu Cys Ser Ser Gly Gly Cys Trp Gly Pro
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Gly Pro Gly Gln Cys Leu Ser Cys Arg Asn Tyr Ser Arg Glu Gly Val
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Cys Val Thr His Cys Asn Val Leu Gln Gly Glu Pro Arg Glu Phe Val
530 535 540

His Glu Ala His Cys Phe Ser Cys His Pro Glu Cys Gln Pro Met Glu
545 550 555 560

Gly Thr Ser Thr Cys Asn Gly Ser Gly Asp Ala Cys Ala Arg Cys
565 570 575

Ala His Phe Arg Asp Gly Pro His Cys Val Asn Ser Cys Pro His Gly
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Ile Leu Gly Ala Lys Gly Pro Ile Tyr Lys Tyr Pro Asp Ala Gln Asn
595 600 605

Glu Cys Arg Pro Cys His Glu Asn Cys Thr Gln Gly Cys Lys Gly Pro
610 615 620

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645 650 655

Leu Gly Gly Ser Phe Leu Tyr Trp Arg Gly Arg Arg Ile Gln Asn Lys
660 665 670

Arg Ala Met Arg Arg Tyr Leu Glu Arg Gly Glu Ser Ile Glu Pro Leu
675 680 685

Asp Pro Ser Glu Lys Ala Asn Lys Val Leu Ala Arg Ile Phe Lys Glu
690 695 700

Thr Glu Leu Arg Lys Leu Lys Val Leu Gly Ser Gly Val Phe Gly Thr
705 710 715 720

Val His Lys Gly Ile Trp Ile Pro Glu Gly Glu Ser Ile Lys Ile Pro
725 730 735

Val Cys Ile Lys Val Ile Glu Asp Lys Ser Gly Arg Gln Ser Phe Gln
740 745 750

Ala Val Thr Asp His Met Leu Ala Val Gly Ser Leu Asp His Ala His
755 760 765

Ile Val Arg Leu Leu Gly Leu Cys Pro Gly Ser Ser Leu Gln Leu Val
770 775 780

Thr Gln Tyr Leu Pro Leu Gly Ser Leu Leu Asp His Val Arg Gln His
785 790 800

Arg Glu Thr Leu Gly Pro Gln Leu Leu Asn Trp Gly Val Gln Ile
805 810 815

Ala Lys Gly Met Tyr Tyr Leu Glu Glu His Ser Met Val His Arg Asp
820 825 830

Leu Ala Leu Arg Asn Val Met Leu Lys Ser Pro Ser Gln Val Gln Val
835 840 845

Ala Asp Phe Gly Val Ala Asp Leu Leu Pro Pro Asp Asp Lys Gln Leu
850 855 860

Leu His Ser Glu Ala Lys Thr Pro Ile Lys Trp Met Ala Leu Glu Ser
865 870 875 880

Ile His Phe Gly Lys Tyr Thr His Gln Ser Asp Val Trp Ser Tyr Gly
885 890 895

Val Thr Val Trp Glu Leu Met Thr Phe Gly Ala Glu Pro Tyr Ala Gly
900 905 910

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Ile Asp Lys Phe Ile Asn Cys Thr Lys Ile Asn Gly Asn Leu Ile Phe
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Leu Val Thr Gly Ile His Gly Asp Pro Tyr Asn Ala Ile Glu Ala Ile
 370 375 380

Asp Pro Glu Lys Leu Asn Val Phe Arg Thr Val Arg Glu Ile Thr Gly
 385 390 395 400

Phe Leu Asn Ile Gln Ser Trp Pro Pro Asn Met Thr Asp Phe Ser Val
 405 410 415

Phe Ser Asn Leu Val Thr Ile Gly Gly Arg Val Leu Tyr Ser Gly Leu
 420 425 430

Ser Leu Leu Ile Leu Lys Gln Gln Gly Ile Thr Ser Leu Gln Phe Gln
 435 440 445

Ser Leu Lys Glu Ile Ser Ala Gly Asn Ile Tyr Ile Thr Asp Asn Ser
 450 455 460

Asn Leu Cys Tyr Tyr His Thr Ile Asn Trp Thr Thr Leu Phe Ser Thr
 465 470 475 480

Ile Asn Gln Arg Ile Val Ile Arg Asp Asn Arg Lys Ala Glu Asn Cys
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Thr Ala Glu Gly Met Val Cys Asn His Leu Cys Ser Ser Asp Gly Cys
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Trp Gly Pro Gly Pro Asp Gln Cys Leu Ser Cys Arg Arg Phe Ser Arg
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Gly Arg Ile Cys Ile Glu Ser Cys Asn Leu Tyr Asp Gly Glu Phe Arg
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Glu Phe Glu Asn Gly Ser Ile Cys Val Glu Cys Asp Pro Gln Cys Glu
545 550 555 560

Lys Met Glu Asp Gly Leu Leu Thr Cys His Gly Pro Gly Pro Asp Asn
565 570 575

Cys Thr Lys Cys Ser His Phe Lys Asp Gly Pro Asn Cys Val Glu Lys
580 585 590

Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser Phe Ile Phe Lys Tyr Ala
595 600 605

Asp Pro Asp Arg Glu Cys His Pro Cys His Pro Asn Cys Thr Gln Gly
610 615 620

Cys Asn Gly Pro Thr Ser His Asp Cys Ile Tyr Tyr Pro Trp Thr Gly
625 630 635 640

His Ser Thr Leu Pro Gln His Ala Arg Thr Pro Leu Ile Ala Ala Gly
645 650 655

Val Ile Gly Gly Leu Phe Ile Leu Val Ile Val Gly Leu Thr Phe Ala
660 665 670

Val Tyr Val Arg Arg Lys Ser Ile Lys Lys Lys Arg Ala Leu Arg Arg
675 680 685

Phe Leu Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly Thr Ala
690 695 700

Pro Asn Gln Ala Gln Leu Arg Ile Leu Lys Glu Thr Glu Leu Lys Arg
705 710 715 720

Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys Gly Ile
725 730 735

Trp Val Pro Glu Gly Glu Thr Val Lys Ile Pro Val Ala Ile Lys Ile
740 745 750

Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn Val Glu Phe Met Asp Glu
755 760 765

Ala Leu Ile Met Ala Ser Met Asp His Pro His Leu Val Arg Leu Leu
770 775 780

Gly Val Cys Leu Ser Pro Thr Ile Gln Leu Val Thr Gln Leu Met Pro
785 790 795 800

His Gly Cys Leu Leu Glu Tyr Val His Glu His Lys Asp Asn Ile Gly
805 810 815

Ser Gln Leu Leu Leu Asn Trp Cys Val Gln Ile Ala Lys Gly Met Met
820 825 830

Tyr Leu Glu Glu Arg Arg Leu Val His Arg Asp Leu Ala Ala Arg Asn
835 840 845

Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe Gly Leu
850 855 860

Ala Arg Leu Leu Glu Gly Asp Glu Lys Glu Tyr Asn Ala Asp Gly Gly
865 870 875 880

Lys Met Pro Ile Lys Trp Met Ala Leu Glu Cys Ile His Tyr Arg Lys
885 890 895

Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Ile Trp Glu
900 905 910

Leu Met Thr Phe Gly Gly Lys Pro Tyr Asp Gly Ile Pro Thr Arg Glu
915 920 925

Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro Pro Ile
930 935 940

Cys Thr Ile Asp Val Tyr Met Val Met Val Lys Cys Trp Met Ile Asp
945 950 955 960

Ala Asp Ser Arg Pro Lys Phe Lys Glu Leu Ala Ala Glu Phe Ser Arg
965 970 975

Met Ala Arg Asp Pro Gln Arg Tyr Leu Val Ile Gln Gly Asp Asp Arg
980 985 990

Met Lys Leu Pro Ser Pro Asn Asp Ser Lys Phe Phe Gln Asn Leu Leu
995 1000 1005

Asp Glu Glu Asp Leu Glu Asp Met Met Asp Ala Glu Glu Tyr Leu
1010 1015 1020

Val Pro Gln Ala Phe Asn Ile Pro Pro Pro Ile Tyr Thr Ser Arg
1025 1030 1035

Ala Arg Ile Asp Ser Asn Arg Ser Glu Ile Gly His Ser Pro Pro
1040 1045 1050

Pro Ala Tyr Thr Pro Met Ser Gly Asn Gln Phe Val Tyr Arg Asp
1055 1060 1065

Asn Phe Asn Asp Ser Gly Ala Cys Val Thr Gln Cys Pro Gln Thr Phe				
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gtc tac aat cca acc acc ttt caa ctg gaa cac aac ttc aat gca aag				816
Val Tyr Asn Pro Thr Thr Phe Gln Leu Glu His Asn Phe Asn Ala Lys				
260	265	270		
tac acg tat gga gca ttc tgt gtt aag aaa tgt cca cat aac ttc gtg				864
Tyr Thr Tyr Gly Ala Phe Cys Val Lys Lys Cys Pro His Asn Phe Val				
275	280	285		
gta gat tcc agt tct tgt gta cga gcc tgc cct agt tct aag atg gaa				912
Val Asp Ser Ser Ser Cys Val Arg Ala Cys Pro Ser Ser Lys Met Glu				
290	295	300		
gta gaa gaa aat ggg att aaa atg tgt aag cct tgc acc gat att tgc				960
Val Glu Glu Asn Gly Ile Lys Met Cys Lys Pro Cys Thr Asp Ile Cys				
305	310	315	320	
ccc aaa gca tgt gat gga atc ggc acg gga tca ctg atg tct gct cag				1008
Pro Lys Ala Cys Asp Gly Ile Gly Thr Gly Ser Leu Met Ser Ala Gln				
325	330	335		
act gtg gat tca agt aac att gac aaa ttc ata aac tgc aca aag atc				1056
Thr Val Asp Ser Ser Asn Ile Asp Lys Phe Ile Asn Cys Thr Lys Ile				
340	345	350		
aat ggc aat ctc atc ttt ctt gtc act ggc att cat gga gac cct tac				1104
Asn Gly Asn Leu Ile Phe Leu Val Thr Gly Ile His Gly Asp Pro Tyr				
355	360	365		
aat gct att gac gcc ata gat cca gag aaa ctg aat gtc ttt cgg act				1152
Asn Ala Ile Asp Ala Ile Asp Pro Glu Lys Leu Asn Val Phe Arg Thr				
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gtc aga gaa ata aca ggt ttc ctg aac ata cag tct tgg ccc cca aat				1200
Val Arg Glu Ile Thr Gly Phe Leu Asn Ile Gln Ser Trp Pro Pro Asn				
385	390	395	400	
atg aca gat ttc agt gtt ttc tcc aac ctc gtc aca att gga gga aga				1248
Met Thr Asp Phe Ser Val Phe Ser Asn Leu Val Thr Ile Gly Gly Arg				
405	410	415		
gtc ctc tac agt ggt ctc tca ttg ctg atc ctc aaa caa caa ggt atc				1296
Val Leu Tyr Ser Gly Leu Ser Leu Leu Lys Gln Gln Gly Ile				
420	425	430		
act tcc cta cag ttc cag tct ctg aag gaa atc agt gcg ggc aat atc				1344
Thr Ser Leu Gln Phe Gln Ser Leu Lys Glu Ile Ser Ala Gly Asn Ile				
435	440	445		
tac atc act gac aac agc aac ctg tgt tat tac cat acc att aac tgg				1392
Tyr Ile Thr Asp Asn Ser Asn Leu Cys Tyr Tyr His Thr Ile Asn Trp				
450	455	460		
aca aca ctc ttc agc acc att aac cag aga ata gtg atc cga gat aac				1440
Thr Thr Leu Phe Ser Thr Ile Asn Gln Arg Ile Val Ile Arg Asp Asn				
465	470	475	480	
aga aga gct gag aat tgt act gct gaa ggc atg gta tgc aac cac ctg				1488
Arg Arg Ala Glu Asn Cys Thr Ala Glu Gly Met Val Cys Asn His Leu				
485	490	495		
tgt tca aat gat ggt tgt tgg gga cct ggg ccg gac cag tgc ctg tca				1536
Cys Ser Asn Asp Gly Cys Trp Gly Pro Gly Pro Asp Gln Cys Leu Ser				
500	505	510		
tgt cgg cgc ttc agc agg gga aag atc tgc ata gag tct tgc aac ctt				1584

Gly Gly Phe Ala Ala Glu Gln Gly Val Ser Val Pro Tyr Arg Ala
1070 1075 1080

Pro Thr Ser Thr Ile Pro Glu Ala Pro Val Ala Gln Gly Ala Thr
1085 1090 1095

Ala Glu Ile Phe Asp Asp Ser Cys Cys Asn Gly Thr Leu Arg Lys
1100 1105 1110

Pro Val Ala Pro His Val Gln Glu Asp Ser Ser Thr Gln Arg Tyr
1115 1120 1125

Ser Ala Asp Pro Thr Val Phe Ala Pro Glu Arg Ser Pro Arg Gly
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Glu Leu Asp Glu Glu Gly Tyr Met Thr Pro Met Arg Asp Lys Pro
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Lys Gln Glu Tyr Leu Asn Pro Val Glu Glu Asn Pro Phe Val Ser
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Arg Arg Lys Asn Gly Asp Leu Gln Ala Leu Asp Asn Pro Glu Tyr
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His Asn Ala Ser Asn Gly Pro Pro Lys Ala Glu Asp Glu Tyr Val
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Ala Glu Tyr Leu Lys Asn Asn Ile Leu Ser Met Pro Glu Lys Ala
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Lys Lys Ala Phe Asp Asn Pro Asp Tyr Trp Asn His Ser Leu Pro
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Pro Arg Ser Thr Leu Gln His Pro Asp Tyr Leu Gln Glu Tyr Ser
1250 1255 1260

Thr Lys Tyr Phe Tyr Lys Gln Asn Gly Arg Ile Arg Pro Ile Val
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tgt gac tcc cag tgt gag aaa atg gaa gat gga ctc ctc aca tgc cat Cys Asp Ser Gln Cys Glu Lys Met Glu Asp Gly Leu Leu Thr Cys His 545 550 555 560		1680
gga ccg gga cct gac aac tgc aca aag tgc tct cat ttt aag gat ggt Gly Pro Gly Pro Asp Asn Cys Thr Lys Cys Ser His Phe Lys Asp Gly 565 570 575		1728
cca aac tgt gtg gag aaa tgt cca gat ggc cta cag gga gca aac agt Pro Asn Cys Val Glu Lys Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser 580 585 590		1776
ttc att ttt aag tat gca gat cag gat cgg gag tgc cac cct tgc cat Phe Ile Phe Lys Tyr Ala Asp Gln Asp Arg Glu Cys His Pro Cys His 595 600 605		1824
cca aac tgc acc cag ggg tgt aac ggt ccc act agt cat gac tgc att Pro Asn Cys Thr Gln Gly Cys Asn Gly Pro Thr Ser His Asp Cys Ile 610 615 620		1872
tac tac cca tgg acg ggc cat tcc act tta cca caa cac gct aga act Tyr Tyr Pro Trp Thr Gly His Ser Thr Leu Pro Gln His Ala Arg Thr 625 630 635 640		1920
cca ctg att gca gcc gga gtc att gga ggc ctc ttc atc ctg gtg atc Pro Leu Ile Ala Ala Gly Val Ile Gly Gly Leu Phe Ile Leu Val Ile 645 650 655		1968
atg gct ttg aca ttt gct gtc tat gtc aga aga aag agc atc aaa aag Met Ala Leu Thr Phe Ala Val Tyr Val Arg Arg Lys Ser Ile Lys Lys 660 665 670		2016
aaa cgt gct ttg agg aga ttc ctg gag aca gag ctg gta gag ccc tta Lys Arg Ala Leu Arg Arg Phe Leu Glu Thr Glu Leu Val Glu Pro Leu 675 680 685		2064
act ccc agt ggc acg gca ccc aat caa gct caa ctt cgc att ttg aag Thr Pro Ser Gly Thr Ala Pro Asn Gln Ala Gln Leu Arg Ile Leu Lys 690 695 700		2112
gaa acc gaa cta aag agg gta aag gtc ctt ggc tcg gga gct ttt gga Glu Thr Glu Leu Lys Arg Val Lys Val Leu Gly Ser Gly Ala Phe Gly 705 710 715 720		2160
acc gtt tat aaa ggt att tgg gtg cct gaa ggt gaa aca gtg aaa atc Thr Val Tyr Lys Gly Ile Trp Val Pro Glu Gly Glu Thr Val Lys Ile 725 730 735		2208
cct gtg gct ata aag atc ctc aat gaa aca act ggc ccc aaa gcc aac Pro Val Ala Ile Lys Ile Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn 740 745 750		2256
gtg gag ttc atg gat gag gct ctg atc atg gca agt atg gat cac cca Val Glu Phe Met Asp Glu Ala Leu Ile Met Ala Ser Met Asp His Pro 755 760 765		2304
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Val Thr Gln Leu Met Pro His Gly Cys Leu Leu Asp Tyr Val His Glu	
785 790 795 800	
cac aag gat aac att gga tca cag ctg ctg ttg aac tgg tgt gtc cag	2448
His Lys Asp Asn Ile Gly Ser Gln Leu Leu Leu Asn Trp Cys Val Gln	
805 810 815	
att gct aag gga atg atg tac cta gaa gaa aga cgg ctt gtt cat cgg	2496
Ile Ala Lys Gly Met Met Tyr Leu Glu Glu Arg Arg Leu Val His Arg	
820 825 830	
gat ctg gca gcc cgc aat gtc tta gtg aaa tct cca aat cat gtt aaa	2544
Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys	
835 840 845	
atc aca gat ttt gga ctg gcc cgg ctc ttg gaa gga gat gaa aaa gaa	2592
Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Glu Gly Asp Glu Lys Glu	
850 855 860	
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Tyr Asn Ala Asp Gly Lys Met Pro Ile Lys Trp Met Ala Leu Glu	
865 870 875 880	
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Cys Ile His Tyr Arg Lys Phe Thr His Gln Ser Asp Val Trp Ser Tyr	
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gga att cca acc cga gaa atc ccc gat tta ctg gag aaa gga gag cgt	2784
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ctg cct cag cct ccc atc tgc act att gat gtt tac atg gtc atg gtc	2832
Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Val Met Val	
930 935 940	
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Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Lys Glu Leu	
945 950 955 960	
gct gct gag ttt tca aga atg gct aga gac cct caa aga tac cta gtt	2928
Ala Ala Glu Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Tyr Leu Val	
965 970 975	
att cag ggt gat gat cgt atg aag ctt ccc agt cca aat gac agc aaa	2976
Ile Gln Gly Asp Asp Arg Met Lys Leu Pro Ser Pro Asn Asp Ser Lys	
980 985 990	
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Phe Phe Gln Asn Leu Leu Asp Glu Glu Asp Leu Glu Asp Met Met Asp	
995 1000 1005	
gct gag gaa tat ttg gtc ccc cag gct ttc aac ata cct cct ccc	3069
Ala Glu Glu Tyr Leu Val Pro Gln Ala Phe Asn Ile Pro Pro Pro	
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Ile Tyr Thr Ser Arg Thr Arg Ile Asp Ser Asn Arg Ser Glu Ile	
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Gly His Ser Pro Pro Ala Tyr Thr Pro Met Ser Gly Asn Gln	
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Phe Val Tyr Gln Asp Gly Gly	Phe Ala Thr Gln Gln	Gly Met Pro	
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Met Pro Tyr Arg Ala Thr Thr	Ser Thr Ile Pro Glu	Ala Pro Val	
1070	1075	1080	
gct cag ggt gca acg gct gag	atg ttt gat gac tcc	tgc tgt aat	3294
Ala Gln Gly Ala Thr Ala Glu	Met Phe Asp Asp Ser	Cys Cys Asn	
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ggt acc cta cga aag cca gtg	gca ccc cat gtc caa	gag gac agt	3339
Gly Thr Leu Arg Lys Pro Val	Ala Pro His Val Gln	Glu Asp Ser	
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Ser Thr Gln Arg Tyr Ser Ala	Asp Pro Thr Val Phe	Ala Pro Glu	
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cgg aat cct cga gga gaa ctg	gat gaa gaa ggc tac	atg act cca	3429
Arg Asn Pro Arg Gly Glu Leu	Asp Glu Glu Gly Tyr	Met Thr Pro	
1130	1135	1140	
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Met His Asp Lys Pro Lys Gln	Glu Tyr Leu Asn Pro	Val Glu Glu	
1145	1150	1155	
aac cct ttt gtg tcc cga agg	aag aat gga gat ctt	caa gct tta	3519
Asn Pro Phe Val Ser Arg Arg	Lys Asn Gly Asp Leu	Gln Ala Leu	
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Asp Asn Pro Glu Tyr His Ser	Ala Ser Ser Gly Pro	Pro Lys Ala	
1175	1180	1185	
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Glu Asp Glu Tyr Val Asn Glu	Pro Leu Tyr Leu Asn	Thr Phe Ala	
1190	1195	1200	
aat gcc ttg ggg agt gca gag	tac atg aaa aac agt	gta ctg tct	3654
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gtg cca gag aaa gcc aag aaa	gca ttt gac aac ccc	gac tac tgg	3699
Val Pro Glu Lys Ala Lys Lys	Ala Phe Asp Asn Pro	Asp Tyr Trp	
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Asn His Ser Leu Pro Pro Arg	Ser Thr Leu Gln His	Pro Asp Tyr	
1235	1240	1245	
ctg cag gaa tac agc aca aaa	tat ttt tat aaa gag	aat gga cg	3789
Leu Gln Glu Tyr Ser Thr Lys	Tyr Phe Tyr Lys Gln	Asn Gly Arg	
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1265	1270	1275	
tcg ctg aag cct ggc act atg	ctg ccc cct ccg ccc	tac aga cac	3879
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Arg Asn Thr Val Val			
1295			

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35 40 45

Val Met Gly Asn Leu Glu Ile Thr Ser Ile Glu His Asn Arg Asp Leu
50 55 60

Ser Phe Leu Arg Ser Ile Arg Glu Val Thr Gly Tyr Val Leu Val Ala
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Leu Asn Gln Phe Arg Tyr Leu Pro Leu Glu Asn Leu Arg Ile Ile Arg
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Gly Thr Lys Leu Tyr Glu Asp Arg Tyr Ala Leu Ala Ile Phe Leu Asn
100 105 110

Tyr Arg Lys Asp Gly Asn Phe Gly Leu Gln Glu Leu Gly Leu Lys Asn
115 120 125

Leu Thr Glu Ile Leu Asn Gly Gly Val Tyr Val Asp Gln Asn Lys Phe
130 135 140

Leu Cys Tyr Ala Asp Thr Ile His Trp Gln Asp Ile Val Arg Asn Pro
145 150 155 160

Trp Pro Ser Asn Met Thr Leu Val Ser Thr Asn Gly Ser Ser Gly Cys
165 170 175

Gly Arg Cys His Lys Ser Cys Thr Gly Arg Cys Trp Gly Pro Thr Glu
180 185 190

Asn His Cys Gln Thr Leu Thr Arg Thr Val Cys Ala Glu Gln Cys Asp
195 200 205

Gly Arg Cys Tyr Gly Pro Tyr Val Ser Asp Cys Cys His Arg Glu Cys
210 215 220

Ala Gly Gly Cys Ser Gly Pro Lys Asp Thr Asp Cys Phe Ala Cys Met
225 230 235 240

Asn Phe Asn Asp Ser Gly Ala Cys Val Thr Gln Cys Pro Gln Thr Phe
 245 250 255

Val Tyr Asn Pro Thr Thr Phe Gln Leu Glu His Asn Phe Asn Ala Lys
 260 265 270

Tyr Thr Tyr Gly Ala Phe Cys Val Lys Lys Cys Pro His Asn Phe Val
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Val Asp Ser Ser Ser Cys Val Arg Ala Cys Pro Ser Ser Lys Met Glu
 290 295 300

Val Glu Glu Asn Gly Ile Lys Met Cys Lys Pro Cys Thr Asp Ile Cys
 305 310 315 320

Pro Lys Ala Cys Asp Gly Ile Gly Thr Gly Ser Leu Met Ser Ala Gln
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Thr Val Asp Ser Ser Asn Ile Asp Lys Phe Ile Asn Cys Thr Lys Ile
 340 345 350

Asn Gly Asn Leu Ile Phe Leu Val Thr Gly Ile His Gly Asp Pro Tyr
 355 360 365

Asn Ala Ile Asp Ala Ile Asp Pro Glu Lys Leu Asn Val Phe Arg Thr
 370 375 380

Val Arg Glu Ile Thr Gly Phe Leu Asn Ile Gln Ser Trp Pro Pro Asn
 385 390 395 400

Met Thr Asp Phe Ser Val Phe Ser Asn Leu Val Thr Ile Gly Gly Arg
 405 410 415

Val Leu Tyr Ser Gly Leu Ser Leu Leu Ile Leu Lys Gln Gln Gly Ile
 420 425 430

Thr Ser Leu Gln Phe Gln Ser Leu Lys Glu Ile Ser Ala Gly Asn Ile
 435 440 445

Tyr Ile Thr Asp Asn Ser Asn Leu Cys Tyr Tyr His Thr Ile Asn Trp
 450 455 460

Thr Thr Leu Phe Ser Thr Ile Asn Gln Arg Ile Val Ile Arg Asp Asn
 465 470 475 480

Arg Arg Ala Glu Asn Cys Thr Ala Glu Gly Met Val Cys Asn His Leu
 485 490 495

Cys Ser Asn Asp Gly Cys Trp Gly Pro Gly Pro Asp Gln Cys Leu Ser
 500 505 510

Cys Arg Arg Phe Ser Arg Gly Lys Ile Cys Ile Glu Ser Cys Asn Leu
515 520 525

Tyr Asp Gly Glu Phe Arg Glu Phe Glu Asn Gly Ser Ile Cys Val Glu
530 535 540

Cys Asp Ser Gln Cys Glu Lys Met Glu Asp Gly Leu Leu Thr Cys His
545 550 555 560

Gly Pro Gly Pro Asp Asn Cys Thr Lys Cys Ser His Phe Lys Asp Gly
565 570 575

Pro Asn Cys Val Glu Lys Cys Pro Asp Gly Leu Gln Gly Ala Asn Ser
580 585 590

Phe Ile Phe Lys Tyr Ala Asp Gln Asp Arg Glu Cys His Pro Cys His
595 600 605

Pro Asn Cys Thr Gln Gly Cys Asn Gly Pro Thr Ser His Asp Cys Ile
610 615 620

Tyr Tyr Pro Trp Thr Gly His Ser Thr Leu Pro Gln His Ala Arg Thr
625 630 635 640

Pro Leu Ile Ala Ala Gly Val Ile Gly Gly Leu Phe Ile Leu Val Ile
645 650 655

Met Ala Leu Thr Phe Ala Val Tyr Val Arg Arg Lys Ser Ile Lys Lys
660 665 670

Lys Arg Ala Leu Arg Arg Phe Leu Glu Thr Glu Leu Val Glu Pro Leu
675 680 685

Thr Pro Ser Gly Thr Ala Pro Asn Gln Ala Gln Leu Arg Ile Leu Lys
690 695 700

Glu Thr Glu Leu Lys Arg Val Lys Val Leu Gly Ser Gly Ala Phe Gly
705 710 715 720

Thr Val Tyr Lys Gly Ile Trp Val Pro Glu Gly Glu Thr Val Lys Ile
725 730 735

Pro Val Ala Ile Lys Ile Leu Asn Glu Thr Thr Gly Pro Lys Ala Asn
740 745 750

Val Glu Phe Met Asp Glu Ala Leu Ile Met Ala Ser Met Asp His Pro
755 760 765

His Leu Val Arg Leu Leu Gly Val Cys Leu Ser Pro Thr Ile Gln Leu
770 775 780

Val Thr Gln Leu Met Pro His Gly Cys Leu Leu Asp Tyr Val His Glu
 785 790 795 800

 His Lys Asp Asn Ile Gly Ser Gln Leu Leu Leu Asn Trp Cys Val Gln
 805 810 815

 Ile Ala Lys Gly Met Met Tyr Leu Glu Glu Arg Arg Leu Val His Arg
 820 825 830

 Asp Leu Ala Ala Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys
 835 840 845

 Ile Thr Asp Phe Gly Leu Ala Arg Leu Leu Glu Gly Asp Glu Lys Glu
 850 855 860

 Tyr Asn Ala Asp Gly Gly Lys Met Pro Ile Lys Trp Met Ala Leu Glu
 865 870 875 880

 Cys Ile His Tyr Arg Lys Phe Thr His Gln Ser Asp Val Trp Ser Tyr
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 Gly Val Thr Ile Trp Glu Leu Met Thr Phe Gly Gly Lys Pro Tyr Asp
 900 905 910

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 915 920 925

 Leu Pro Gln Pro Pro Ile Cys Thr Ile Asp Val Tyr Met Val Met Val
 930 935 940

 Lys Cys Trp Met Ile Asp Ala Asp Ser Arg Pro Lys Phe Lys Glu Leu
 945 950 955 960

 Ala Ala Glu Phe Ser Arg Met Ala Arg Asp Pro Gln Arg Tyr Leu Val
 965 970 975

 Ile Gln Gly Asp Asp Arg Met Lys Leu Pro Ser Pro Asn Asp Ser Lys
 980 985 990

 Phe Phe Gln Asn Leu Leu Asp Glu Glu Asp Leu Glu Asp Met Met Asp
 995 1000 1005

 Ala Glu Glu Tyr Leu Val Pro Gln Ala Phe Asn Ile Pro Pro Pro
 1010 1015 1020

 Ile Tyr Thr Ser Arg Thr Arg Ile Asp Ser Asn Arg Ser Glu Ile
 1025 1030 1035

 Gly His Ser Pro Pro Pro Ala Tyr Thr Pro Met Ser Gly Asn Gln
 1040 1045 1050

Phe Val Tyr Gln Asp Gly Gly Phe Ala Thr Gln Gln Gly Met Pro
 1055 1060 1065
 Met Pro Tyr Arg Ala Thr Thr Ser Thr Ile Pro Glu Ala Pro Val
 1070 1075 1080
 Ala Gln Gly Ala Thr Ala Glu Met Phe Asp Asp Ser Cys Cys Asn
 1085 1090 1095
 Gly Thr Leu Arg Lys Pro Val Ala Pro His Val Gln Glu Asp Ser
 1100 1105 1110
 Ser Thr Gln Arg Tyr Ser Ala Asp Pro Thr Val Phe Ala Pro Glu
 1115 1120 1125
 Arg Asn Pro Arg Gly Glu Leu Asp Glu Glu Gly Tyr Met Thr Pro
 1130 1135 1140
 Met His Asp Lys Pro Lys Gln Glu Tyr Leu Asn Pro Val Glu Glu
 1145 1150 1155
 Asn Pro Phe Val Ser Arg Arg Lys Asn Gly Asp Leu Gln Ala Leu
 1160 1165 1170
 Asp Asn Pro Glu Tyr His Ser Ala Ser Ser Gly Pro Pro Lys Ala
 1175 1180 1185
 Glu Asp Glu Tyr Val Asn Glu Pro Leu Tyr Leu Asn Thr Phe Ala
 1190 1195 1200
 Asn Ala Leu Gly Ser Ala Glu Tyr Met Lys Asn Ser Val Leu Ser
 1205 1210 1215
 Val Pro Glu Lys Ala Lys Lys Ala Phe Asp Asn Pro Asp Tyr Trp
 1220 1225 1230
 Asn His Ser Leu Pro Pro Arg Ser Thr Leu Gln His Pro Asp Tyr
 1235 1240 1245
 Leu Gln Glu Tyr Ser Thr Lys Tyr Phe Tyr Lys Gln Asn Gly Arg
 1250 1255 1260
 Ile Arg Pro Ile Val Ala Glu Asn Pro Glu Tyr Leu Ser Glu Phe
 1265 1270 1275
 Ser Leu Lys Pro Gly Thr Met Leu Pro Pro Pro Pro Tyr Arg His
 1280 1285 1290
 Arg Asn Thr Val Val
 1295

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US05/04968

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/00; G01N 33/53; A61K 38/00; C07K 1/00, 2/00, 4/00, 5/00, 7/00, 14/00, 16/00, 17/00
 US CL : 435/4, 7.1; 530/300, 350, 385, 386, 387.1, 387.3; 436/64, 86

According to International Patent Classification (IPC) or to both national classification and JPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/4, 7.1; 530/300, 350, 385, 386, 387.1, 387.3; 436/64, 86

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

West and Medline

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ROBERTS, R.B. et al. Modeling the cancer patient with genetically engineered mice: prediction of toxicity from molecule-targeted therapies. February 2004, Vol 5, pages 115-120.	1-28

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "B" earlier application or patent published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T"

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X"

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y"

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&"

document member of the same patent family

Date of the actual completion of the international search

30 August 2005 (30.08.2005)

Date of mailing of the international search report

27 JAN 2006

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